

Claims

1. A nucleic acid molecule encoding an inactive form of the
5 human transcription initiation factor TIF-IA.

2. The nucleic acid molecule of claim 1, wherein the human
transcription initiation factor TIF-IA is not or not
completely posttranslationally modified.

10 3. The nucleic acid molecule of claim 2, wherein the serine
residue at position 633 and/or 649 is replaced by another
amino acid residue.

15 4. The nucleic acid molecule of claim 3, wherein the serine
residue at position 649 is replaced by an alanine residue.

5. The nucleic acid molecule of claim 2, wherein at least one
amino acid residue being part of the recognition motif for a
20 phosphatase or kinase comprising the serine residue at
position 633 and/or 649 is replaced by another amino acid
residue.

25 6. The nucleic acid molecule of claim 2, wherein the serine
residue at position 44 and/or 199 is replaced by another amino
acid residue.

7. The nucleic acid molecule of claim 6, wherein the serine
residue at position 44 is replaced by an alanine residue or an
30 aspartic acid residue and/or the serine residue at position
199 is replaced by an aspartic acid residue.

8. The nucleic acid molecule of claim 2, wherein at least one
amino acid residue being part of the recognition motif for a
35 phosphatase or kinase comprising the serine residue at
position 44 and/or 199 is replaced by another amino acid

residue.

9. A recombinant vector containing the nucleic acid molecule of any one of claims 1 to 8.

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10. The recombinant vector of claim 8 wherein the nucleic acid molecule is operatively linked to regulatory elements allowing transcription and synthesis of a translatable RNA in prokaryotic and/or eukaryotic host cells.

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11. The recombinant vector of claim 9 or 10 which is a vaccinia based expression vector.

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12. A recombinant host cell which contains the recombinant vector of any one of claims 9 to 11.

13. The recombinant host cell of claim 12, which is a mammalian cell, a bacterial cell, an insect cell or a yeast cell.

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14. An inactive human transcription initiation factor TIF-IA which is encoded by a nucleic acid molecule of any one of claims 1 to 8.

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15. A method of producing an inactive human transcription initiation factor TIF-IA comprising:

(a) culturing the recombinant host cell of claim 12 or 13 under conditions such that said TIF-IA is expressed; and
(b) recovering said TIF-IA.

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16. An inactive human transcription initiation factor TIF-IA produced by the method of claim 15.

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17. A transgenic non-human animal comprising at least one nucleic acid molecule of any one of claims 1 to 8 or the recombinant vector of any one of claims 9 to 11.

18. A cell line comprising at least one nucleic acid molecule of any one of claims 1 to 8 or the recombinant vector of any one of claims 9 to 11.

5 19. The transgenic non-human animal of claim 17 or the cell line of claim 18 further comprising at least one wild type allele of the TIF-IIA encoding gene.

10 20. The transgenic non-human animal of claim 17 or 19 which is a mouse or rat.

() 21. A pharmaceutical composition comprising a nucleic acid molecule of any one of claims 1 to 8, a TIF-IIA polypeptide of claim 14 or 16, or a recombinant vector of any one of claims 9 15 to 11 and a pharmaceutically acceptable excipient, diluent or carrier.

22. A method for identifying compounds capable of inhibiting the conversion of an inactive pre-form of TIF-IIA into a 20 biologically active form, said method comprising the steps of:

- (a) contacting a cell which expresses TIF-IIA and all factors required for said conversion of said TIF-IIA with a compound to be screened; and
(b) determining if the compound inhibits the conversion of an inactive pre-form of TIF-IIA into a biologically active form.

23. Use of a nucleic acid molecule of any one of claims 1 to 8, a TIF-IIA polypeptide of claim 14 or 16, a recombinant vector of 30 any one of claims 9 to 11, a compound identified according to the method of claim 22, or a compound capable of inactivating TIF-IIA for the preparation of a medicament for treatment of a disease which is associated with an increased cell proliferation.

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24. Use according to claim 23, wherein the disease is a tumor.